REMARKS

Attached hereto is a marked-up version of the changes made to the claims by the current amendment. The attached page is captioned "Version with markings to show changes made." Applicants reserve the right to prosecute non-elected subject matter in subsequent divisional applications.

I Comments Regarding Restriction Requirement

Newly added claims 45-47, 49, 50, 52 and 54-61 correspond to previously elected "antibody" subject matter and are fully supported in the Specification as filed. Claims 48, 51, 53, 62 and 63 are methods of using the claimed antibodies and, hence, should also be considered. See the Commissioner's Notice in the Official Gazette of March 26, 1996, entitled "Guidance on Treatment of Product and Process Claims in light of In re Ochiai, In re Brouwer and 35 U.S.C. § 103(b)", by which the Patent Office has set forth criteria for rejoining non-elected method claims upon allowance of product claims.

II Enablement Rejection under 35 U.S.C. § 112, first paragraph

Claims 28, 30-31, 33 and 35-42 stand rejected under 35 U.S.C. 112, first paragraph allegedly for lacking an enabling disclosure with respect to variants and biologically active and immunogenic fragments of SEQ ID NO:1. The Examiner has specifically stated that "The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in **scope** with the claims." (March 13, 2002 Office Action, at page 6). The Examiner further states "The specification does not teach how to make and use *any* antibody that binds to a polypeptide comprising a) *any* naturally-occurring amino acid sequence having at least 90% sequence identity to the amino acid sequence of SEQ ID NO: 1, b) *any* biologically active fragment of the polypeptide "having:" an

amino acid sequence of SEQ ID NO:1, c) *any* immunogenic fragment of the polypeptide "having" an amino acid sequence of SEQ ID NO: 1 since neither the structure nor function of any amino acid sequence mentioned above is provided." (March 13, 2002 Office Action, at page 6)

Applicants thank Examiner for her time in examination of the application but respectfully traverse this rejection. The Specification provides extensive teaching on how to make and use antibodies, see for example page 6, lines 30-36, page 24, lines 34-36, page 30, lines 17-24. Further, the Specification describes how to make variants to the amino acids sequence of SEQ ID NO:1, including variants having 90% sequence identity to SEQ ID NO:1, as well as to fragments of SEQ ID NO:1 having biological or immunogenic activity (see page 2, lines 30-36, page 6, lines 14-19 and page 11, lines 22-29. Thus on this basis, one skilled in the art would know how to make and use antibodies to variants and fragments of SEQ ID NO:1. This is further evidenced by the fact that the specification describes the production of antibodies to fragments and hence, variants of P5CR proteins at, for example, page 6, lines 32-33.

Further, Applicants submit that the invention contemplates a number of specific uses for antibodies which bind amino acid sequences that are variants or fragments of SEQ ID NO: 1. For example, the skilled artisan could use different antibodies to purify protein having an 1) amino acid sequence that is a variant sequence of SEQ ID NO: 1 verses 2) a P5CR protein sequence having the exact sequence SEQ ID NO: 1 (See Example XIII., page 44, lines 29-36). In another use, antibodies to variants or fragments of the amino acid sequence of SEQ ID NO: 1 can be used for drug screening purposes (see page 34 lines 30-36 and page 35 lines 1-5). Note lines 4-5 on page 35 which state that "antibodies can be used to detect the presence of any peptide which shares one or more antigenic determinants with P5CRH." Additionally, antibodies which specifically bind to variants or fragments of SEQ ID NO: 1, can be used for example in 2D-Page analysis for expression profiling related to toxicology testing, drug discovery and disease diagnosis. Thus based on the multiple uses contemplated in the Specification, Applicants submit that the skilled artisan would readily know how to use antibodies to a variant or fragment of the sequence of SEQ ID NO: 1.

While Applicants respectfully traverse the above rejection, in order to expedite prosecute of the Application and soley for purposes thereof, Applicants present new claim 45 which includes the functional language of "1-pyrroline-5-carboxylate reductase activity". In addition, the

fragment language has been deleted from the claims, rendering these issues moot. Applicants believe this claim and subsequent related claims are allowable in their present form.

III. Written Description Rejection Under 35 U.S.C. § 112, first paragraph

Claims 28, 30-31, 33 and 35-42 are rejected under 35 U.S.C. 112, first paragraph, as allegedly containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor, at the time the application was filed, had possession of the claimed invention.

Applicants respectfully traverse this rejection. The Specification provides written description of antibodies to variant to the amino sequence of SEQ ID NO:1 including variants having 90% sequence identity to SEQ ID NO:1 as well as to fragments of SEQ ID NO:1 having biological or immunogenic activity (see page 2, lines 30-36, page 6, lines 14-19 and page 11, lines 22-29). This is further evidenced by the fact that the specification describes the production of antibodies to fragments and hence, variants of P5CR proteins at, for example, page 6, lines 32 to page 7, line 1.

However in order to expedite prosecute of the Application, and soley for purposes thereof, Applicants present new claim 45 which includes the functional language of "1-pyrroline-5-carboxylate reductase activity". In addition, the "fragment language" has been deleted from the claims, rendering these issues moot. Applicants believe this claim and subsequent related claims are allowable in their present form.

IV Double Patenting Rejections:

Claims 28, 31, 33 and 35-40 stand rejected under the judicially created doctrine of obviousness-type double patenting. Applicants hereby submit a Terminal Disclaimer to address these rejections. Accordingly, withdrawal of these rejections is respectfully requested.

CONCLUSION

In light of the above amendments and remarks, Applicants submit that the present application is fully in condition for allowance, and request that the Examiner withdraw the outstanding rejections. Applicants respectfully submit that the present application is fully in condition for allowance, and respectfully request such action. If the Examiner contemplates other action, Applicants respectfully request a telephone conference at the Examiner's earliest convenience before the issuance of any subsequent action. Applicants invite the Examiner to contact the undersigned at (650) 843-4866.

Please charge any required fees, including extension of time fees under 37 CFR § 1.17 to, Deposit Account No. **09-0108**.

Respectfully submitted,

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VERSION WITH MARKINGS TO SHOW CHANGES MADE

IN THE SPECIFICATION

The paragraph beginning at page 1, line 2 has been amended as follows:

This patent application is a divisional application of [USSN 09/565,910, filed May 5, 2000, which is a divisional application of USPN 6,100,075 issued August 8, 2000, all of which applications and patents are hereby incorporated by reference.] U.S. Patent Application Serial No. 09/565,910, filed May 5, 2000, now U.S. Patent No. 6,268,192, entitled "Delta 1-pyrroline-5-carboxylate reductase homolog" issued July 31, 2001 which is a divisional application of U.S. Patent Application Serial No. 09/099,676, filed June 18, 1998 now U.S. Patent No. 6,100,075, entitled "Delta 1-pyrroline-5-carboxylate reductase homolog " issued August 8, 2000, all incorporated herein by reference.

IN THE CLAIMS:

Claims 1-3 and 28-44 have been cancelled.

The following new claims 45-63 have been added:

45. (New) An isolated antibody which specifically binds to a polypeptide selected from the group consisting of:

a) a polypeptide comprising the amino acid sequence of SEQ ID NO:1, and

b) a polypeptide comprising a naturally occurring amino acid sequence at least 90% identical to the amino acid sequence of SEQ ID NO:1, said naturally occurring amino acid sequence having 1-pyrroline-5-carboxylate reductase activity.

46. (New) The antibody of claim 45 which specifically binds to a polypeptide

comprising the amino acid sequence of SEQ ID NO:1.

47. (New) The antibody of claim 45 which specifically binds to a polypeptide comprising a naturally-occurring amino acid sequence at least 90% identical to the amino acid sequence of SEQ ID NO:1, said naturally occurring amino acid sequence having1-pyrroline-5-carboxylate reductase activity.

48. (New) A diagnostic test for a condition or disease associated with the expression of P5CR in a biological sample, the method comprising:

a) combining the biological sample with an antibody of claim 45, under conditions suitable for the antibody to bind the polypeptide and form an antibody:polypeptide complex, and

b) detecting the complex, wherein the presence of the complex correlates with the presence of the polypeptide in the biological sample.

49. (New) The antibody of claim 45, wherein the antibody is:

a) a chimeric antibody,

b) a single chain antibody,

c) a Fab fragment,

d) a $F(ab')_2$ fragment, or

e) a humanized antibody.

50. (New) A composition comprising an antibody of claim 45 and an acceptable excipient.

51. (New) A method of diagnosing a condition or disease associated with the expression of P5CRH in a subject, comprising administering to said subject an effective amount of the composition of claim 50.

52. (New) A composition of claim 50, wherein the antibody is labeled.

53. (New) A method of diagnosing a condition or disease associated with the expression of P5CR in a subject, comprising administering to said subject an effective amount of the composition of claim 52.

54. (New) A method of preparing a polyclonal antibody with the specificity of the antibody of claim 45, the method comprising:

a) immunizing an animal with a polypeptide having the amino acid sequence of SEQ ID NO:1, or an immunogenic fragment thereof, under conditions to elicit an antibody response,

b) isolating antibodies from said animal, and

c) screening the isolated antibodies with the polypeptide, thereby identifying a polyclonal antibody which binds specifically to a polypeptide having the amino acid sequence of SEQ ID NO:1.

55. (New) A polyclonal antibody produced by a method of claim 54.

56. (New) A composition comprising the polyclonal antibody of claim 55 and a suitable carrier.

57. (New) A method of making a monoclonal antibody with the specificity of the antibody of claim 45, the method comprising:

a) immunizing an animal with a polypeptide having the amino acid sequence of SEQ ID NO:1, or an immunogenic fragment thereof, under conditions to elicit an antibody response,

b) isolating antibody producing cells from the animal,

c) fusing the antibody producing cells with immortalized cells to form monoclonal antibody-producing hybridoma cells,

d) culturing the hybridoma cells, and

e) isolating from the culture monoclonal antibody which binds specifically to a polypeptide having the amino acid sequence of SEQ ID NO:1.

58. (New) A monoclonal antibody produced by a method of claim 57.

59. (New) A composition comprising the monoclonal antibody of claim 58 and a suitable carrier.

60. (New) The antibody of claim 45, wherein the antibody is produced by screening a Fab expression library.

61. (New) The antibody of claim 45, wherein the antibody is produced by screening a recombinant immunoglobulin library.

62. (New) A method of detecting a polypeptide having the amino acid sequence of SEQ ID NO:1 in a sample, the method comprising:

a) incubating the antibody of claim 45 with a sample under conditions to allow specific binding of the antibody and the polypeptide, and

b) detecting specific binding, wherein specific binding indicates the presence of a polypeptide having the amino acid sequence of SEQ ID NO:1 in the sample.

63. (New) A method of purifying a polypeptide having the amino acid sequence of SEQ ID NO:1 from a sample, the method comprising:

a) incubating the antibody of claim 45 with a sample under conditions to allow specific binding of the antibody and the polypeptide, and

b) separating the antibody from the sample and obtaining the purified polypeptide having the amino acid sequence of SEQ ID NO:1.